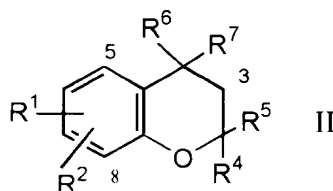


4. A compound of the formula:



wherein

R^1 is OH, $O(CH_2)_{1-2}OH$, OCH_2CO_2H , CO_2H , $O-Z-C(O)NH(CH_2)_{1-6}R^{17}$ or $OCH_2-4-Phe-C(O)NH(CH_2)_{1-6}R^{17}$;

R^2 is H or lower alkyl;

R^3 is H, alkyl, aryl, or arylalkyl;

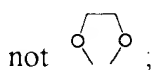
R^4 and R^5 are each independently H, lower alkyl, or substituted lower alkyl where the substituents are 1-3 alkoxy, aryl, substituted aryl, carboalkoxy, carboxamido or di-loweralkylamido; or

R^4 and R^5 taken together are $-(CH_2)_n-$, $-(CH_2)_2-O-(CH_2)_2-$, $-CH_2-O-(CH_2)_3-$, $-(CH_2)_2-NR^8-CH_2-$, $-CH_2-NR^8-(CH_2)_m-$, $-(CH_2)_2CH(NHR^8)(CH_2)_2-$, $-(CH_2)_2-S(O)_{0-2}-(CH_2)_2-$, or $-CH_2CH(N-loweralkyl)(CH_2)_2CHCH_2-$;

one of R^6 and R^7 is H and the other is H, OH, or $N(CH_2)_{1-6}R^{14}R^{15}$; or

R^6 and R^7 taken together are or with the proviso that

when R^1 is -OH and R^2 is -H, R^6 and R^7 are not -H and -OH or when taken together are



R^8 is H, $COOR^9$, $CONHR^{10}$, $CSNHR^{11}$, COR^{12} , SO_2R^{13} , lower alkyl, aryl lower alkyl, heteroaryl, or heteroaryl lower alkyl, wherein aryl is optionally substituted with 1-3 substituents selected from lower alkyl, lower alkoxy, halo, CN, NH_2 , $COOH$, $CONH_2$,

carboalkoxy, and mono- or di-lower alkylamino and wherein heteroaryl is a mono- or bicyclic heteroaromatic ring system of 5 to 10 members including 1 to 3 heteroatoms selected from O, N, and S and 0-3 substituents selected from halo, amino, cyano, lower alkyl, carboalkoxy, CONH₂, and S-lower alkyl;

R⁹ is lower alkyl, aryl, aryl lower alkyl, heteroaryl, aryl substituted by 1-3 substituents selected from alkyl, alkenyl, alkoxy, methylene dioxy, and halo, or a 5- to 6-membered heterocyclic ring containing O or N as a heteroatom, wherein heteroaryl is a heteroaromatic ring of 5 to 6 members including 1 to 2 heteroatoms selected from O, N, and S and 0-2 substituents selected from lower alkyl, dialkylamino, lower alkoxy, and halo;

R¹⁰ and R¹¹ are each independently lower alkyl, aryl, aryl lower alkyl, or aryl substituted by 1-3 substituents selected from lower alkyl, halo, alkoxy and haloalkyl;

R¹² is lower alkyl, aryl, heteroaryl, aryl lower alkyl, heteroaryl lower alkyl, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N-lower alkyl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, sulfamoyl, lower alkyl sulfamoyl, cyano, and phenyl;

R¹³ is lower alkyl, aryl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, CN, and haloalkyl;

R¹⁴ is H, alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH₂NR¹⁶C(O)R¹⁶; -C(O)NR¹⁶R¹⁶; -CH₂OC(O)R¹⁶; or -CH₂SC(O)R¹⁶;

R¹⁵ is H, alkyl, -C(O)X, -C(S)X, or -C(NCN)NR³R³;

R¹⁶ is lower alkyl, substituted lower alkyl, aryl, or substituted aryl;

R¹⁷ is H, alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl;

heteroaryl; substituted heteroaryl; heterocycloalkyl; $-\text{CH}_2\text{NR}^{16}\text{C}(\text{O})\text{R}^{16}$, $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{16}$,
 $-\text{CH}_2\text{OC}(\text{O})\text{R}^{16}$; or $-\text{CH}_2\text{SC}(\text{O})\text{R}^{16}$;

X is alkyl, aryl, arylalkyl, O-loweralkyl, or $-\text{NR}^3\text{R}^3$;

Z is $-(\text{CH}_2)_{1-6}-$, optionally substituted with 1-3 lower alkyl; $-\text{CHR}^2-$; $-\text{Phe}-\text{CH}_2-$, where Phe is
 optionally mono-substituted with halogen, lower alkyl, or alkoxy; or heteroarylene- $(\text{CH}_2)-$;

m is 2 or 3, and

n is 4-9;

or a pharmaceutically acceptable salt thereof.

5. A compound of claim 4, wherein R^{12} is sulfamoylphenyl.

6. A compound of claim 4, wherein R^{12} is p-sulfamoylphenyl.

7. A compound of claim 4, wherein:

R^1 is OH, $\text{OCH}_2\text{C}(\text{O})\text{NH}(\text{CH}_2)_{1-6}\text{R}^{17}$, or $\text{OCH}_2-4\text{-Phe}-\text{C}(\text{O})\text{NH}(\text{CH}_2)_{1-6}\text{R}^{17}$;

R^4 and R^5 are each lower alkyl; or

R^4 and R^5 taken together are $-(\text{CH}_2)_5-$, $-(\text{CH}_2)_2-\text{O}-(\text{CH}_2)_2-$, $-(\text{CH}_2)_2-\text{NR}^8-(\text{CH}_2)_2-$,
 $-(\text{CH}_2)_2-\text{CH}(\text{NHR}^8)(\text{CH}_2)_2-$, $-(\text{CH}_2)_2-\text{S}-(\text{CH}_2)_2-$, or $-\text{CH}_2\text{CH}(\text{NCH}_3)(\text{CH}_2)_2\text{CHCH}_2-$;

R^6/R^7 are H/OH or $-\text{S}(\text{CH}_2)_2\text{S}-$;

R^8 is H, COOR^9 , CONHR^{10} , CSNHR^{11} , COR^{12} , SO_2R^{13} , lower alkyl, aryl lower alkyl,
 heteroaryl wherein the heteroatoms include 1 to 3 N atoms and the substituents are halo or
 amino, heteroaryl lower alkyl wherein heteroaryl is 6-membered and the heteroatoms are
 N, or aryl lower alkyl substituted with 1 substituent selected from lower alkyl, alkoxy, and
 halo;

R^9 is lower alkyl, aryl lower alkyl, aryl, tetrahydrofuranyl, tetrahydropyranyl, or aryl
 substituted by 1 to 2 substituents selected from lower alkyl, alkenyl, alkoxy, methylene
 dioxy, and halo;

R^{10} and R^{11} are each independently aryl, aryl lower alkyl, or aryl substituted by 1 substituent selected from lower alkyl, halo, alkoxy, trifluoromethyl, and pentafluoroethyl;

R^{12} is lower alkyl, aryl, aryl lower alkyl, heteroaryl lower alkyl wherein the heteroatoms are N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from S and N lower alkyl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, halo, sulfamoyl, cyano, or phenyl; and

R^{13} is lower alkyl, aryl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

or a pharmaceutically acceptable salt thereof.

38. A compound of claim 4 wherein:

R^1 is $\text{OCH}_2\text{CO}_2\text{H}$;

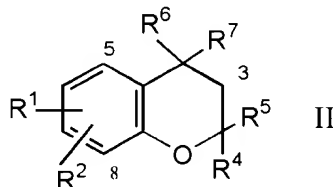
R^2 is -H;

R^4 and R^5 taken together are $-(\text{CH}_2)_2-\text{S}-(\text{O})_2-(\text{CH}_2)_2-$; and

one of R^6 and R^7 is -H and the other is -H or $-\text{N}(\text{CH}_2)_{1-6}\text{R}^{14}\text{R}^{15}$.

The foregoing amended claims effect the following changes:

4. (thrice amended) A compound of the formula:



wherein:

R^1 is OH , $\text{O}(\text{CH}_2)_{1-2}\text{OH}$, $\text{OCH}_2\text{CO}_2\text{H}$, CO_2H , $\text{O}-\text{Z}-\text{C}(\text{O})\text{NH}(\text{CH}_2)_{1-6}\text{R}^{17}$ or $\text{OCH}_2-4\text{-Phe}-\text{C}(\text{O})\text{NH}(\text{CH}_2)_{1-6}\text{R}^{17}$;


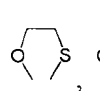



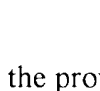
R^2 is H or lower alkyl;

R^3 is H, alkyl, aryl, or arylalkyl;


R^4 and R^5 are each independently H, lower alkyl, or substituted lower alkyl where the substituents are 1-3 alkoxy, aryl, substituted aryl, carboalkoxy, carboxamido or di-loweralkylamido; or

R^4 and R^5 taken together are $-(CH_2)_n-$, $-(CH_2)_2-O-(CH_2)_2-$, $-CH_2-O-(CH_2)_3-$, $-(CH_2)_2-NR^8-(CH_2)_2-$, $-CH_2-NR^8-(CH_2)_m-$, $-(CH_2)_2CH(NHR^8)(CH_2)_2-$, $-(CH_2)_2-S(O)_{0-2}-(CH_2)_2-$, or $-CH_2CH(N-\text{loweralkyl})(CH_2)_2CHCH_2-$;

one of R^6 and R^7 is H and the other is H, OH, or $N(CH_2)_{1-6}R^{14}R^{15}$, or

R^6 and R^7 taken together are $\left[\begin{array}{c} \text{O} \\ \parallel \\ \text{C} \end{array} \right]$, , , , , or  or , with the proviso that

when R^1 is -OH and R^2 is -H, R^6 and R^7 are not -H and -OH or when taken together are

not ;

R^8 is H, $COOR^9$, $CONHR^{10}$, $CSNHR^{11}$, COR^{12} , SO_2R^{13} , lower alkyl, aryl lower alkyl, heteroaryl, or heteroaryl lower alkyl, wherein aryl is optionally substituted with 1-3 substituents selected from lower alkyl, lower alkoxy, halo, CN, NH_2 , $COOH$, $CONH_2$, carboalkoxy, and mono- or di-lower alkylamino and wherein heteroaryl is a mono- or bicyclic heteroaromatic ring system of 5 to 10 members including 1 to 3 heteroatoms selected from O, N, and S and 0-3 substituents selected from halo, amino, cyano, lower alkyl, carboalkoxy, $CONH_2$, and S-lower alkyl;

R^9 is lower alkyl, aryl, aryl lower alkyl, heteroaryl, aryl substituted by 1-3 substituents selected from alkyl, alkenyl, alkoxy, methylene dioxy, and halo, or a 5- to 6-membered heterocyclic ring [wherein the hetero atom is] **containing O or N as a heteroatom**, wherein

heteroaryl is a heteroaromatic ring of 5 to 6 members including 1 to 2 heteroatoms selected from O, N, and S and 0-2 substituents selected from lower alkyl, dialkylamino, lower alkoxy, and halo;

R¹⁰ and R¹¹ are each independently lower alkyl, aryl, aryl lower alkyl, or aryl substituted by 1-3 substituents selected from lower alkyl, halo, alkoxy and haloalkyl;

R¹² is lower alkyl, aryl, heteroaryl, aryl lower alkyl, heteroaryl lower alkyl, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N-lower alkyl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, sulfamoyl, lower alkyl sulfamoyl, cyano, and phenyl;

R¹³ is lower alkyl, aryl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, CN, and haloalkyl;

R¹⁴ is H; alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH₂NR¹⁶C(O)R¹⁶, -C(O)NR¹⁶R¹⁶, -CH₂OC(O)R¹⁶; or -CH₂SC(O)R¹⁶;

R¹⁵ is H, alkyl, -C(O)X, -C(S)X, or -C(NCN)NR³R³;

R¹⁶ is lower alkyl, substituted lower alkyl, aryl, or substituted aryl;

R¹⁷ is H; alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH₂NR¹⁶C(O)R¹⁶, -C(O)NR¹⁶R¹⁶, -CH₂OC(O)R¹⁶; or -CH₂SC(O)R¹⁶;

X is alkyl, aryl, arylalkyl, O-loweralkyl, or -NR³R³;

Z is -(CH₂)₁₋₆-, optionally substituted with 1-3 lower alkyl; -CHR²-; -Phe-CH₂-, where Phe is optionally mono-substituted with halogen, lower alkyl, or alkoxy; or heteroarylene-(CH₂)₂-;

m is 2 or 3; **and**

n is 4-9;

or a pharmaceutically acceptable salt thereof.

5. (once amended) A compound of claim 4 wherein R¹² is sulfamoylphenyl.

6. (once amended) A compound of claim 4 wherein R¹² is *p*-sulfamoylphenyl.

7. (once amended) A compound of claim 4 wherein:

R¹ is OH, OCH₂C(O)NH(CH₂)₁₋₆R¹⁷, or OCH₂-4-Phe-C(O)NH(CH₂)₁₋₆R¹⁷;

R⁴ and R⁵ are each lower alkyl; or

R⁴ and R⁵ taken together are -(CH₂)₅-, -(CH₂)₂-O-(CH₂)₂-, -(CH₂)₂-NR⁸-(CH₂)₂-,
 -(CH₂)₂-CH(NHR⁸)(CH₂)₂-, -(CH₂)₂-S-(CH₂)₂-, or -CH₂CH(NCH₃)(CH₂)₂CHCH₂- ;

R⁶/R⁷ are H/OH [; =O ,] or -S(CH₂)₂S-;

R⁸ is H, COOR⁹, CONHR¹⁰, CSNHR¹¹, COR¹², SO₂R¹³, lower alkyl, aryl lower alkyl, heteroaryl wherein the [ring members] **heteroatoms** include 1 to 3 N atoms and the substituents are halo or amino, heteroaryl lower alkyl wherein heteroaryl is 6-membered and the heteroatoms are N, or aryl lower alkyl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

R⁹ is lower alkyl, aryl lower alkyl, aryl, tetrahydrofuranyl, tetrahydropyranyl, or aryl substituted by 1 to 2 substituents selected from lower alkyl, alkenyl, alkoxy, methylene dioxy, and halo;

R¹⁰ and R¹¹ are each independently aryl, aryl lower alkyl, or aryl substituted by 1 substituent selected from lower alkyl, halo, alkoxy, trifluoromethyl, and pentafluoroethyl;

R¹² is lower alkyl, aryl, aryl lower alkyl, heteroaryl lower alkyl wherein the heteroatoms are N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from S and N

lower alkyl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, halo, sulfamoyl, cyano, or phenyl; **and**

R¹³ is lower alkyl, aryl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

or a pharmaceutically acceptable salt thereof.

38. (once amended) A compound of claim 4 wherein:

R¹ is OCH₂CO₂H;

R² is -H,

R⁴ and R⁵ taken together are -(CH₂)₂-S-(O)₂-(CH₂)₂-; **and**

one of R⁶ and R⁷ is -H and the other is -H or -N(CH₂)₁₋₆R¹⁴R¹⁵ [;

R¹⁴ is -H, and

R¹⁵ is alkyl] .

III. New Claims

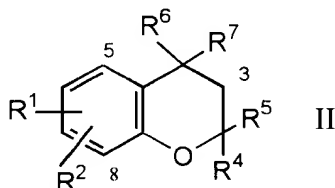
Please add new claims 39-49.

39. A compound of claim 38 wherein:

R¹⁴ is -H, and

R¹⁵ is alkyl.

40. A compound of the formula:



wherein:

R^1 is OCH_2CO_2H ;

R^2 is H;

R^4 and R^5 taken together are $-(CH_2)_2-S(O)_2-(CH_2)_2-$; and

one of R^6 and R^7 is -H and the other is -H or $-N(CH_2)_{1-6}R^{14}R^{15}$,

wherein:

R^{14} is H; alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; $-CH_2NR^{16}C(O)R^{16}$; $-C(O)NR^{16}R^{16}$; $-CH_2OC(O)R^{16}$; or $-CH_2SC(O)R^{16}$;

wherein:

R^{16} is lower alkyl, substituted lower alkyl, aryl, or substituted aryl; and

R^{15} is H, alkyl, $-C(O)X$, $-C(S)X$, or $-C(NCN)NR^3R^3$;

wherein:

X is alkyl, aryl, arylalkyl, O-loweralkyl, or $-NR^3R^3$; and

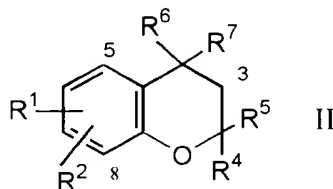
R^3 is H, alkyl, aryl, or arylalkyl.

41. A compound of claim 40, wherein:

R^{14} is -H; and

R^{15} is alkyl.

42. A compound of the formula:



wherein:

R^1 is OH, $O(CH_2)_{1-2}OH$, OCH_2CO_2H , CO_2H , $O-Z-C(O)NH(CH_2)_{1-6}R^{17}$ or $OCH_2-4-Phe-C(O)NH(CH_2)_{1-6}R^{17}$;

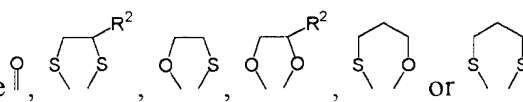
R^2 is H or lower alkyl;

R^3 is H, alkyl, aryl, or arylalkyl;

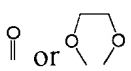
R^4 and R^5 are each independently H, lower alkyl, or substituted lower alkyl where the substituents are 1-3 alkoxy, aryl, substituted aryl, carboalkoxy, carboxamido or di-loweralkylamido; or


R^4 and R^5 taken together are $-(CH_2)_n-$, $-(CH_2)_2-O-(CH_2)_2-$, $-CH_2-O-(CH_2)_3-$, $-(CH_2)_2-NR^8-CH_2-$, $-CH_2-NR^8-(CH_2)_m-$, $-(CH_2)_2CH(NHR^8)(CH_2)_2-$, $-(CH_2)_2-S(O)_{0-2}-(CH_2)_2-$, or $-CH_2CH(N-\text{loweralkyl})(CH_2)_2CHCH_2-$;

one of R^6 and R^7 is H and the other is H, OH, or $N(CH_2)_{1-6}R^{14}R^{15}$; or

R^6 and R^7 taken together are , with the proviso that

when R^1 is -OH and R^2 is -H, R^6 and R^7 are not -H and -OH or when taken together are

not  and when R^1 is $-OCH_2CO_2H$ and R^4 and R^5 are both -H or methyl, R^6 and R^7

taken together is not ;

R^8 is H, $COOR^9$, $CONHR^{10}$, $CSNHR^{11}$, COR^{12} , SO_2R^{13} , lower alkyl, aryl lower alkyl, heteroaryl, or heteroaryl lower alkyl, wherein aryl is optionally substituted with 1-3 substituents selected from lower alkyl, lower alkoxy, halo, CN, NH_2 , $COOH$, $CONH_2$, carboalkoxy, and mono- or di-lower alkylamino and wherein heteroaryl is a mono- or bicyclic heteroaromatic ring system of 5 to 10 members including 1 to 3 heteroatoms selected from O, N, and S and 0-3 substituents selected from halo, amino, cyano, lower

alkyl, carboalkoxy, CONH₂, and S-lower alkyl;

R⁹ is lower alkyl, aryl, aryl lower alkyl, heteroaryl, aryl substituted by 1-3 substituents selected from alkyl, alkenyl, alkoxy, methylene dioxy, and halo, or a 5- to 6-membered heterocyclic ring containing O or N as a heteroatom, wherein heteroaryl is a heteroaromatic ring of 5 to 6 members including 1 to 2 heteroatoms selected from O, N, and S and 0-2 substituents selected from lower alkyl, dialkylamino, lower alkoxy, and halo;

R¹⁰ and R¹¹ are each independently lower alkyl, aryl, aryl lower alkyl, or aryl substituted by 1-3 substituents selected from lower alkyl, halo, alkoxy and haloalkyl;

R¹² is lower alkyl, aryl, heteroaryl, aryl lower alkyl, heteroaryl lower alkyl, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N-lower alkyl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, sulfamoyl, lower alkyl sulfamoyl, cyano, and phenyl;

R¹³ is lower alkyl, aryl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, CN, and haloalkyl;

R¹⁴ is H; alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl, substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH₂NR¹⁶C(O)R¹⁶; -C(O)NR¹⁶R¹⁶; -CH₂OC(O)R¹⁶; or -CH₂SC(O)R¹⁶;

R¹⁵ is H, alkyl, -C(O)X, -C(S)X, or -C(NCN)NR³R³;

R¹⁶ is lower alkyl, substituted lower alkyl, aryl, or substituted aryl;

R¹⁷ is H; alkyl, alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH₂NR¹⁶C(O)R¹⁶; -C(O)NR¹⁶R¹⁶; -CH₂OC(O)R¹⁶; or -CH₂SC(O)R¹⁶;

X is alkyl, aryl, arylalkyl, O-loweralkyl, or -NR³R³;

Z is -(CH₂)₁₋₆-, optionally substituted with 1-3 lower alkyl; -CHR²-, -Phe-CH₂-, where Phe is

optionally mono-substituted with halogen, lower alkyl, or alkoxy; or heteroarylene-(CH₂)-;
 m is 2 or 3; and
 n is 4-9;
 or a pharmaceutically acceptable salt thereof.

43. A compound of claim 42, wherein R¹² is sulfamoylphenyl.

44. A compound of claim 42, wherein R¹² is *p*-sulfamoylphenyl.

45. A compound of claim 42, wherein:

R¹ is OH, OCH₂C(O)NH(CH₂)₁₋₆R¹⁷, or OCH₂-4-Phe-C(O)NH(CH₂)₁₋₆R¹⁷;

R⁴ and R⁵ are each lower alkyl, or

R⁴ and R⁵ taken together are -(CH₂)₅-, -(CH₂)₂-O-(CH₂)₂-, -(CH₂)₂-NR⁸-(CH₂)₂-,
 -(CH₂)₂-CH(NHR⁸)(CH₂)₂-, -(CH₂)₂-S-(CH₂)₂-, or -CH₂CH(NCH₃)(CH₂)₂CHCH₂- ;

R⁶/R⁷ are H/OH; =O, or -S(CH₂)₂S-,

R⁸ is H, COOR⁹, CONHR¹⁰, CSNHR¹¹, COR¹², SO₂R¹³, lower alkyl, aryl lower alkyl, heteroaryl wherein the heteroatoms include 1 to 3 N atoms and the substituents are halo or amino, heteroaryl lower alkyl wherein heteroaryl is 6-membered and the heteroatoms are N, or aryl lower alkyl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

R⁹ is lower alkyl, aryl lower alkyl, aryl, tetrahydrofuranyl, tetrahydropyranyl, or aryl substituted by 1 to 2 substituents selected from lower alkyl, alkenyl, alkoxy, methylene dioxy, and halo;

R¹⁰ and R¹¹ are each independently aryl, aryl lower alkyl, or aryl substituted by 1 substituent selected from lower alkyl, halo, alkoxy, trifluoromethyl, and pentafluoroethyl;

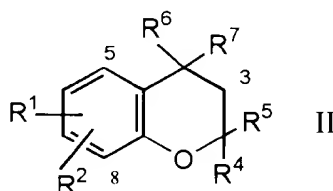
R¹² is lower alkyl, aryl, aryl lower alkyl, heteroaryl lower alkyl wherein the heteroatoms are N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from S and N

lower alkyl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, halo, sulfamoyl, cyano, or phenyl; and

R^{13} is lower alkyl, aryl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

or a pharmaceutically acceptable salt thereof.

46. A compound of the formula:



wherein

R^1 is $O(CH_2)_{1-2}OH$, CO_2H , $O-Z-C(O)NH(CH_2)_{1-6}R^{17}$ or $OCH_2-4-Phe-C(O)NH(CH_2)_{1-6}R^{17}$;

R^2 is H or lower alkyl;

R^3 is H, alkyl, aryl, or arylalkyl;


R^4 and R^5 are each independently H, lower alkyl, or substituted lower alkyl where the substituents are 1-3 alkoxy, aryl, substituted aryl, carboalkoxy, carboxamido or di-loweralkylamido; or

R^4 and R^5 taken together are $-(CH_2)_n-$, $-(CH_2)_2-O-(CH_2)_2-$, $-CH_2-O-(CH_2)_3-$, $-(CH_2)_2-NR^8-CH_2-$, $-CH_2-NR^8-(CH_2)_m-$, $-(CH_2)_2CH(NHR^8)(CH_2)_2-$, $-(CH_2)_2-S(O)_{0-2}-(CH_2)_2-$, or $CH_2CH(N-loweralkyl)(CH_2)_2CHCH_2-$;

one of R^6 and R^7 is H and the other is H, OH, or $N(CH_2)_{1-6}R^{14}R^{15}$; or

R^6 and R^7 taken together are , with the proviso that

when R^1 is $-OH$ and R^2 is $-H$, R^6 and R^7 are not $-H$ and $-OH$ or when taken together are

not  ;

- R^8 is H, COOR^9 , CONHR^{10} , CSNHR^{11} , COR^{12} , SO_2R^{13} , lower alkyl, aryl lower alkyl, heteroaryl, or heteroaryl lower alkyl, wherein aryl is optionally substituted with 1-3 substituents selected from lower alkyl, lower alkoxy, halo, CN, NH_2 , COOH , CONH_2 , carboalkoxy, and mono- or di-lower alkylamino and wherein heteroaryl is a mono- or bicyclic heteroaromatic ring system of 5 to 10 members including 1 to 3 heteroatoms selected from O, N, and S and 0-3 substituents selected from halo, amino, cyano, lower alkyl, carboalkoxy, CONH_2 , and S-lower alkyl;
- R^9 is lower alkyl, aryl, aryl lower alkyl, heteroaryl, aryl substituted by 1-3 substituents selected from alkyl, alkenyl, alkoxy, methylene dioxy, and halo, or a 5- to 6-membered heterocyclic ring containing O or N as a heteroatom, wherein heteroaryl is a heteroaromatic ring of 5 to 6 members including 1 to 2 heteroatoms selected from O, N, and S and 0-2 substituents selected from lower alkyl, dialkylamino, lower alkoxy, and halo;
- R^{10} and R^{11} are each independently lower alkyl, aryl, aryl lower alkyl, or aryl substituted by 1-3 substituents selected from lower alkyl, halo, alkoxy and haloalkyl;
- R^{12} is lower alkyl, aryl, heteroaryl, aryl lower alkyl, heteroaryl lower alkyl, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N-lower alkyl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, sulfamoyl, lower alkyl sulfamoyl, cyano, and phenyl;
- R^{13} is lower alkyl, aryl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, CN, and haloalkyl;
- R^{14} is H; alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; $-\text{CH}_2\text{NR}^{16}\text{C}(\text{O})\text{R}^{16}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{16}$; $-\text{CH}_2\text{OC}(\text{O})\text{R}^{16}$; or $-\text{CH}_2\text{SC}(\text{O})\text{R}^{16}$;

R¹⁵ is H, alkyl, -C(O)X, -C(S)X, or -C(NCN)NR³R³;

R¹⁶ is lower alkyl, substituted lower alkyl, aryl, or substituted aryl;

R¹⁷ is H; alkyl, alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH₂NR¹⁶C(O)R¹⁶; -C(O)NR¹⁶R¹⁶; -CH₂OC(O)R¹⁶, or -CH₂SC(O)R¹⁶;

X is alkyl, aryl, arylalkyl, O-loweralkyl, or -NR³R³;

Z is -(CH₂)₁₋₆-, optionally substituted with 1-3 lower alkyl; -CHR²-; -Phe-CH₂-, where Phe is optionally mono-substituted with halogen, lower alkyl, or alkoxy; or heteroarylene-(CH₂)_n;

m is 2 or 3; and

n is 4-9;

or a pharmaceutically acceptable salt thereof.

47. A compound of claim 46, wherein R¹² is sulfamoylphenyl.

48. A compound of claim 46, wherein R¹² is *p*-sulfamoylphenyl.

49. A compound of claim 46, wherein:

R¹ is OCH₂C(O)NH(CH₂)₁₋₆R¹⁷, or OCH₂-4-Phe-C(O)NH(CH₂)₁₋₆R¹⁷;

R⁴ and R⁵ are each lower alkyl; or

R⁴ and R⁵ taken together are -(CH₂)₅-, -(CH₂)₂-O-(CH₂)₂-, -(CH₂)₂-NR⁸-(CH₂)₂-,
-(CH₂)₂-CH(NHR⁸)(CH₂)₂-, -(CH₂)₂-S-(CH₂)₂-, or $\text{CH}_2\text{CH}(\text{NCH}_3)(\text{CH}_2)_2\text{CHCH}_2$;

R⁶/R⁷ are H/OH; =O, or -S(CH₂)₂S-;

R⁸ is H, COOR⁹, CONHR¹⁰, CSNHR¹¹, COR¹², SO₂R¹³, lower alkyl, aryl lower alkyl, heteroaryl wherein the heteroatoms include 1 to 3 N atoms and the substituents are halo or amino, heteroaryl lower alkyl wherein heteroaryl is 6-membered and the heteroatoms are

N, or aryl lower alkyl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

R⁹ is lower alkyl, aryl lower alkyl, aryl, tetrahydrofuranyl, tetrahydropyranyl, or aryl substituted by 1 to 2 substituents selected from lower alkyl, alkenyl, alkoxy, methylene dioxy, and halo;

R¹⁰ and R¹¹ are each independently aryl, aryl lower alkyl, or aryl substituted by 1 substituent selected from lower alkyl, halo, alkoxy, trifluoromethyl, and pentafluoroethyl;

R¹² is lower alkyl, aryl, aryl lower alkyl, heteroaryl lower alkyl wherein the heteroatoms are N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from S and N lower alkyl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, halo, sulfamoyl, cyano, or phenyl; and

R¹³ is lower alkyl, aryl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

or a pharmaceutically acceptable salt thereof.

Remarks

Status of Claims

1-37	Claims of priority application
1-3 and 15-37	Canceled by preliminary amendment
38	Added by July 24, 2000 amendment
8-14	Canceled without prejudice in this paper
39-49	Added in this paper
4-7 and 39-49	Pending following entry of this paper